

Insight into bioabsorbable stent with clinical and imaging outcomes

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on behalf of the ABSORB investigators

Erasmus MC, the Netherlands

TCT-AP

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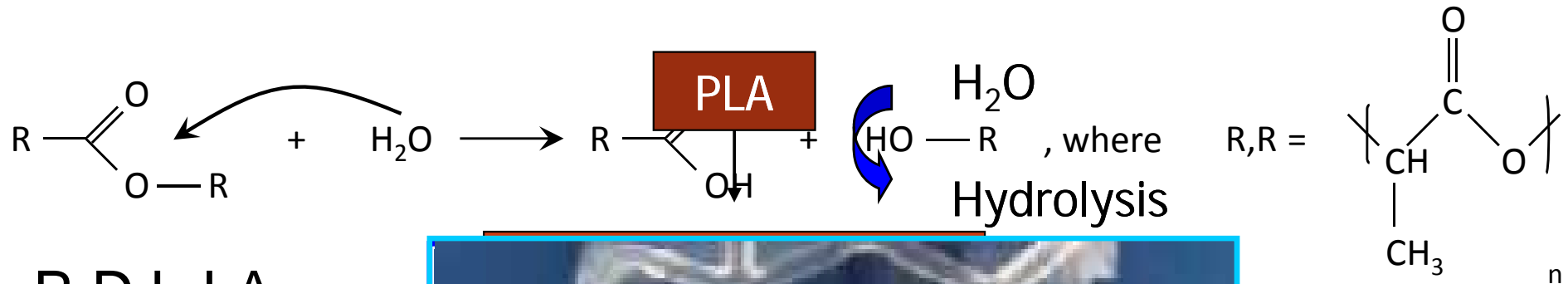
Erasmus MC, the Netherlands

TCT-AP

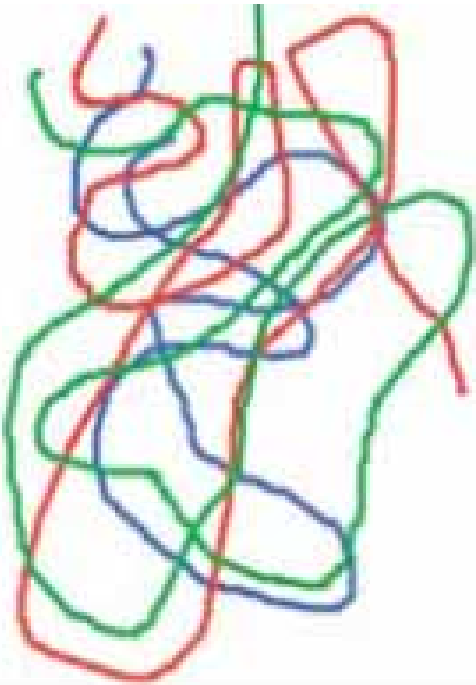
Company	Stent	Development	Pre-clinical	Clinical trials	Post-market
Kyoto Medical	Igaki-Tamai	✓	✓	✓	
Biotronik	Dreams	✓	✓	✓	
Abbott	Absorb	✓	✓	✓	✓
Art	Art18AZ	✓	✓	✓	
Reva Medical	Resolve	✓	✓	✓	
Xenogenics	Ideal biostent	✓	✓		
Orbus Neich	Acute	✓	✓		
Elixir	DESolve	✓	✓	✓	
Amaranth	Amaranth PLLA	✓	✓		
Huaan Biotech	Xinsorb	✓	✓	✓	
S3V	Avatar	✓	✓		
Meril	MeRes	✓	✓		
Zorion Medical	Zorion BRS	✓	✓		
Lifetech	Lifetech Iron	✓	✓		

Polylactide Degradation Mechanism

Hydrolysis via Random Chain Scission of Ester Bonds



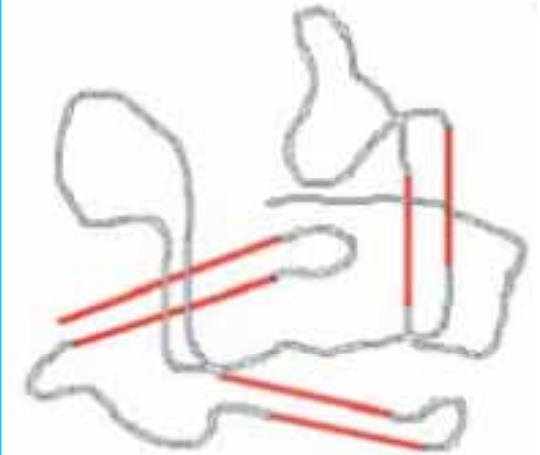
P-D,L-LA



Amorphous

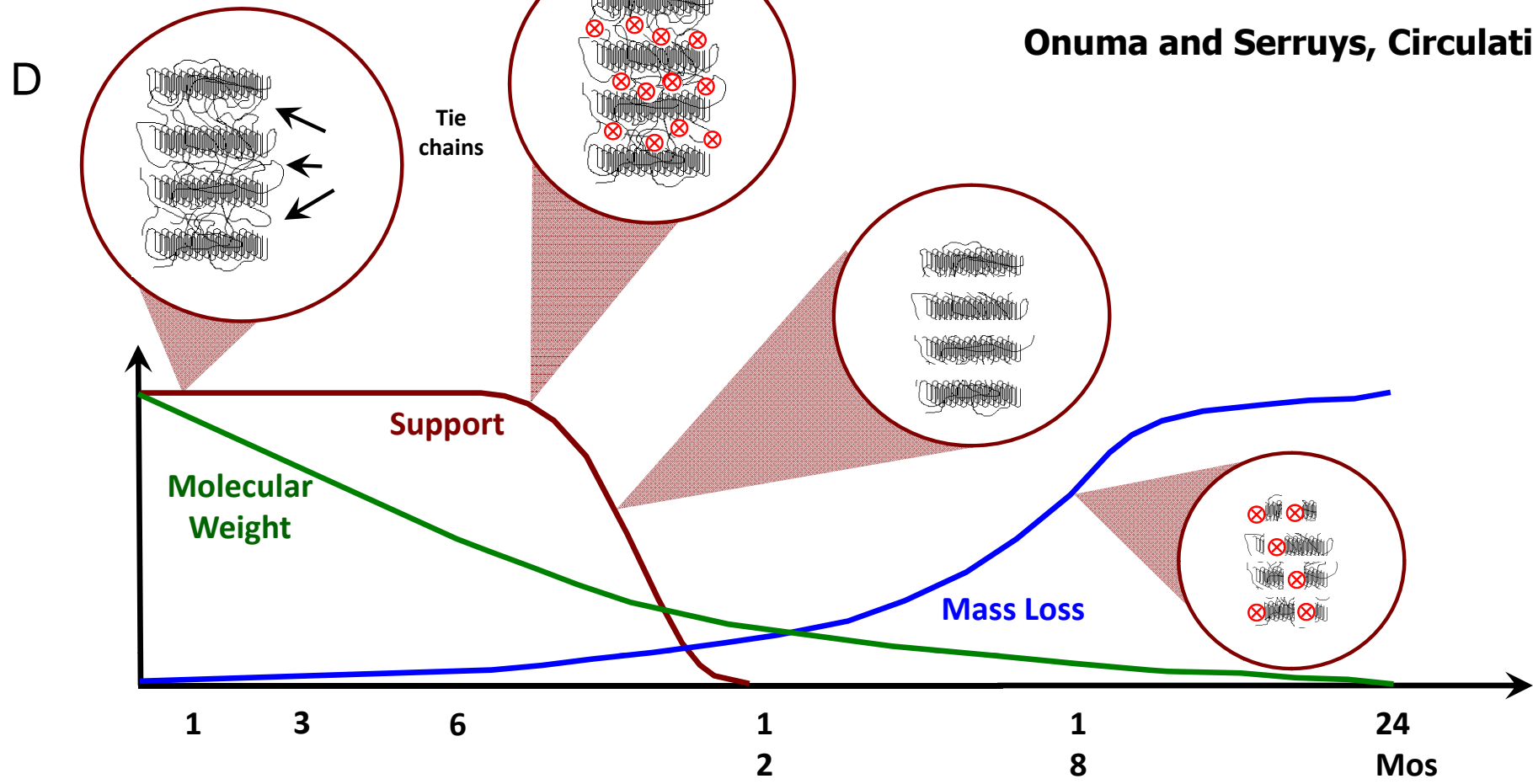
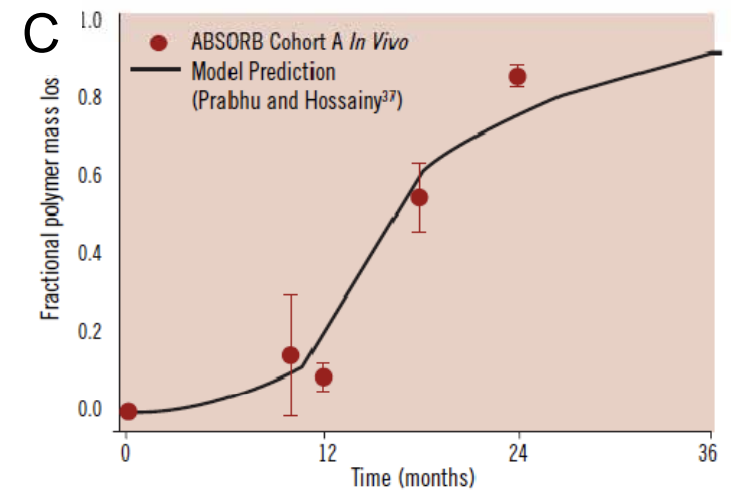
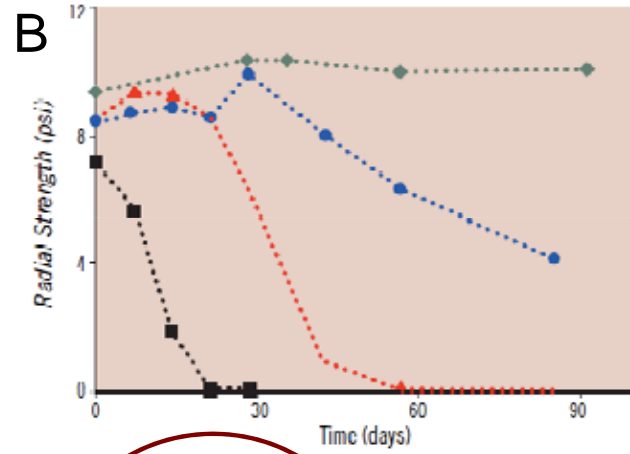
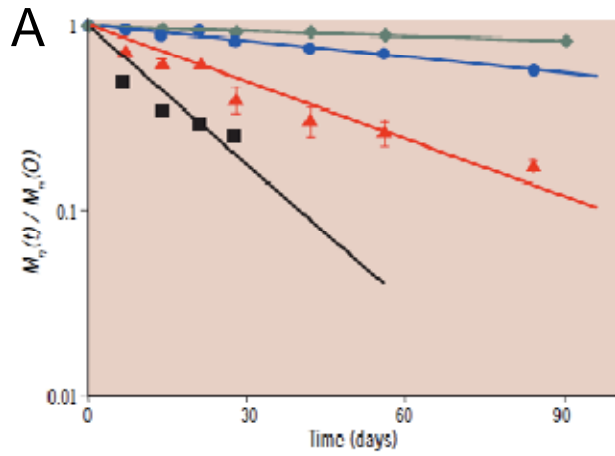


P-L,L-LA



Semicrystalline

#1. The PLLA fully disappears after 2 years, while the mechanical integrity lasts for 6 months



Onuma and Serruys, Circulation 2011

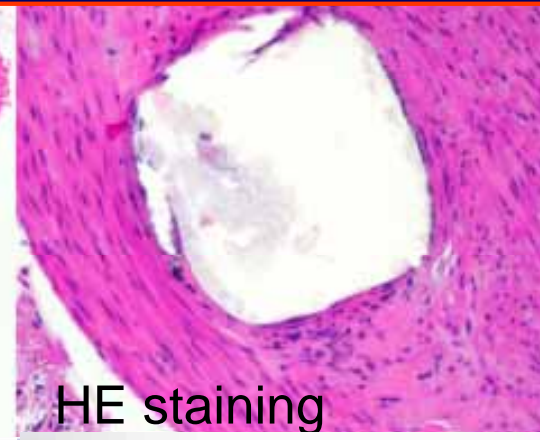


Intracoronary Optical Coherence Tomography and Histology at 1 Month and 2, 3, and 4 Years After Implantation of Everolimus-Eluting Bioresorbable Vascular Scaffolds in a Porcine Coronary Artery Model

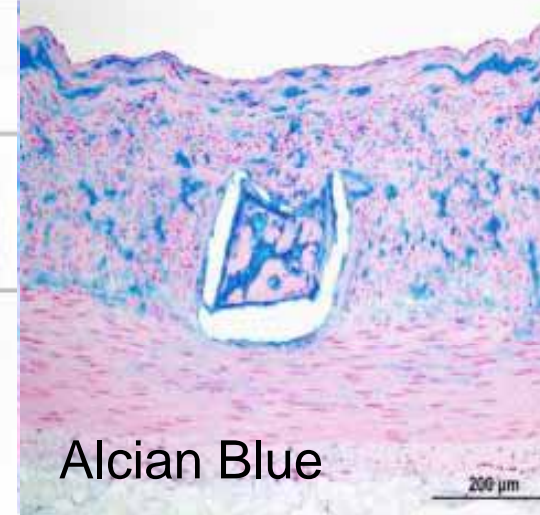
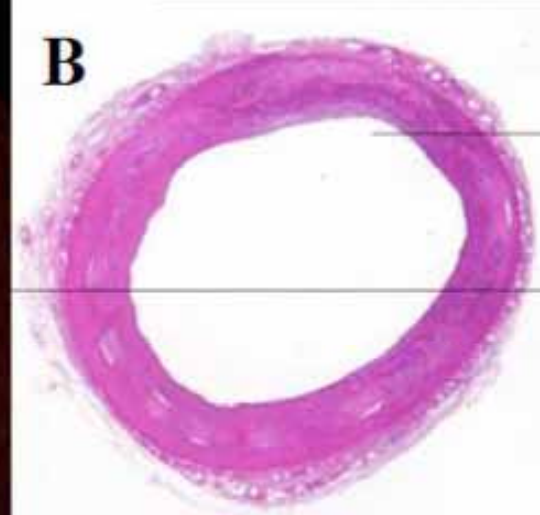
An Attempt to Decipher the Human Optical Coherence Tomography Images in the A Bioabsorbable Everolimus-Eluting Coronary Stent System (ABSORB) Trial

Yoshinobu Onuma, MD*; Patrick Serruys, MD, PhD*; Laura Perkins, DVM, PhD;
Takayuki Okamura, MD; Nieves Gonzalo, MD; Hector M. Garcia-Garcia, MD, PhD;
Evelyn Regar, MD, PhD; Marika Kamberi, PhD; Jennifer C. Powers, BS; Richard Rapoza, PhD;
Heleen van Beusekom, PhD; Willem van der Giessen, MD, PhD; Renu Virmani, PhD

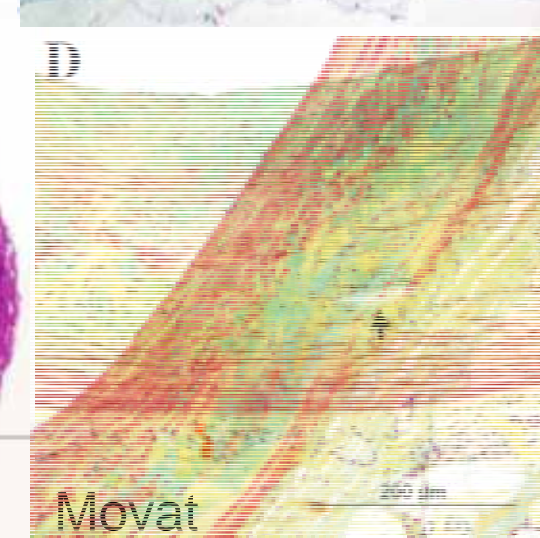
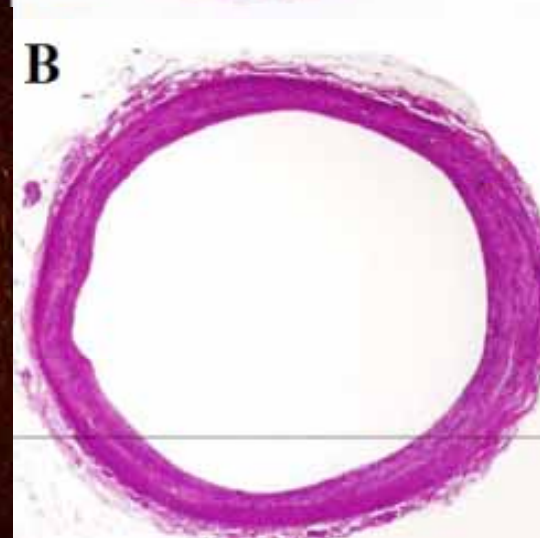
#1. The PLLA fully disappears after 2 years



By chromatography, polymeric struts were no longer detectable



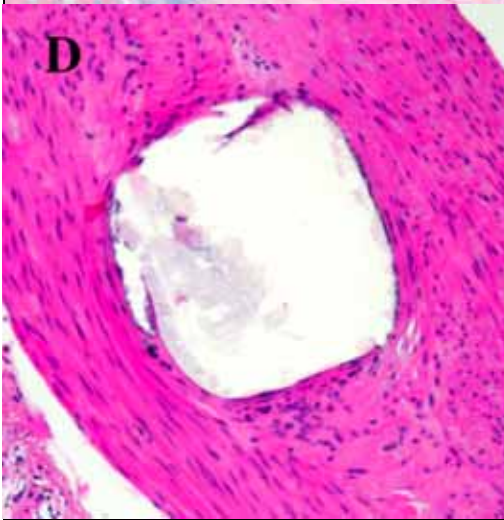
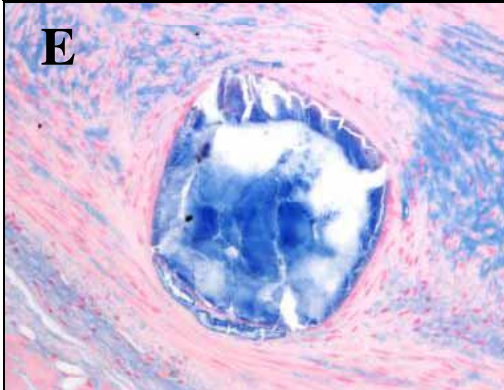
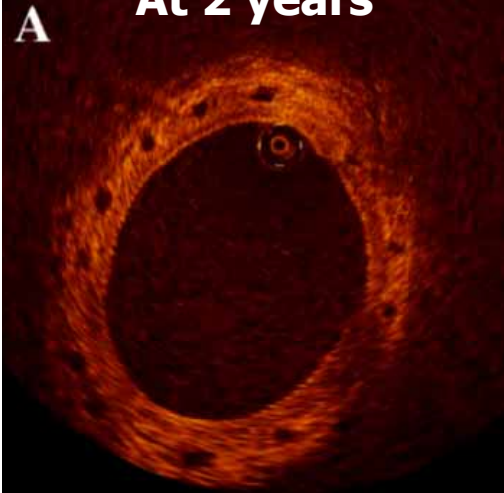
Strut voids were filled with young connective tissue and coalesced with vessel wall.



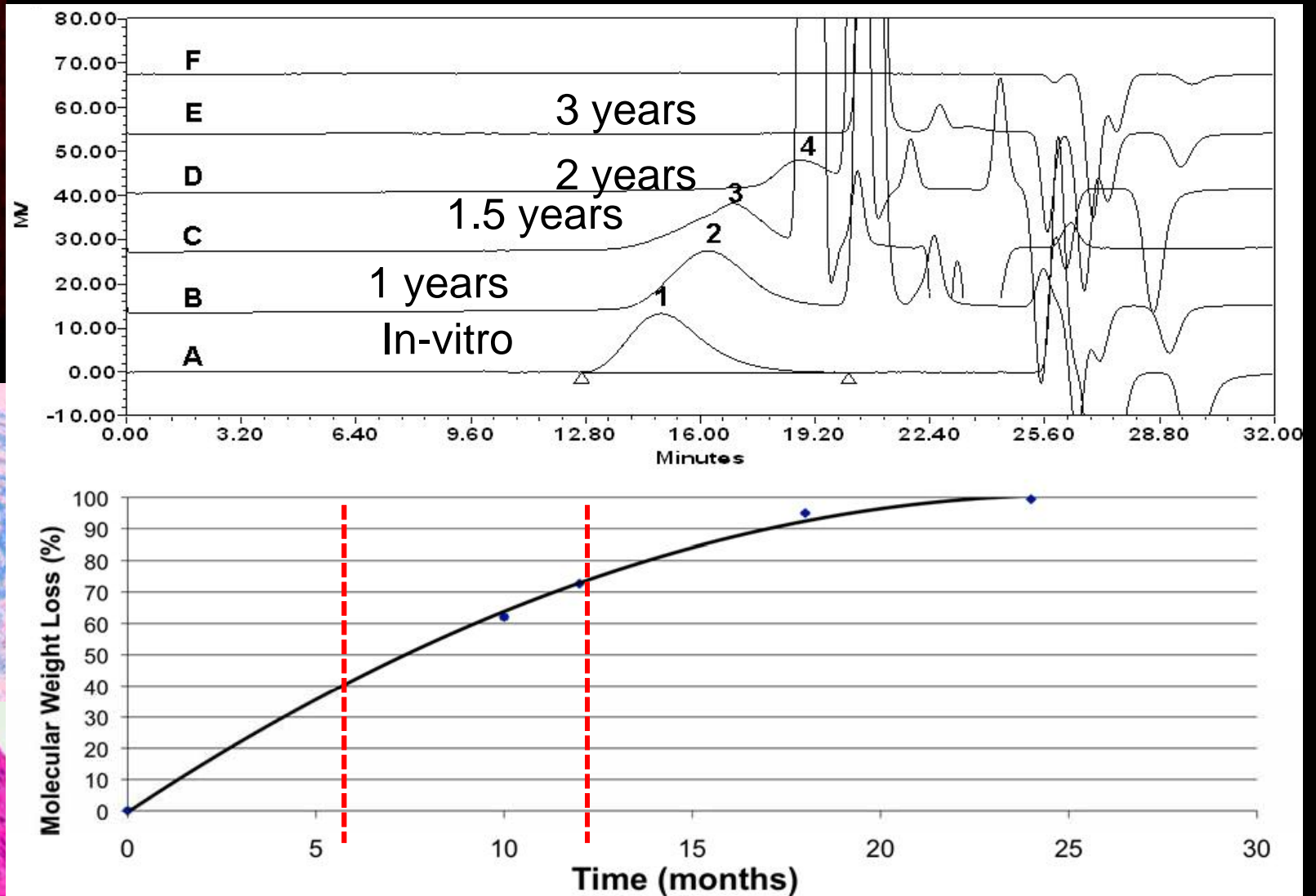
Strut voids are minimally discernible in histology, with localized low density of smooth muscle cells at the presumed site of polymeric struts.

#1. The PLLA fully disappears after 2 years

OCT and Histology At 2 years

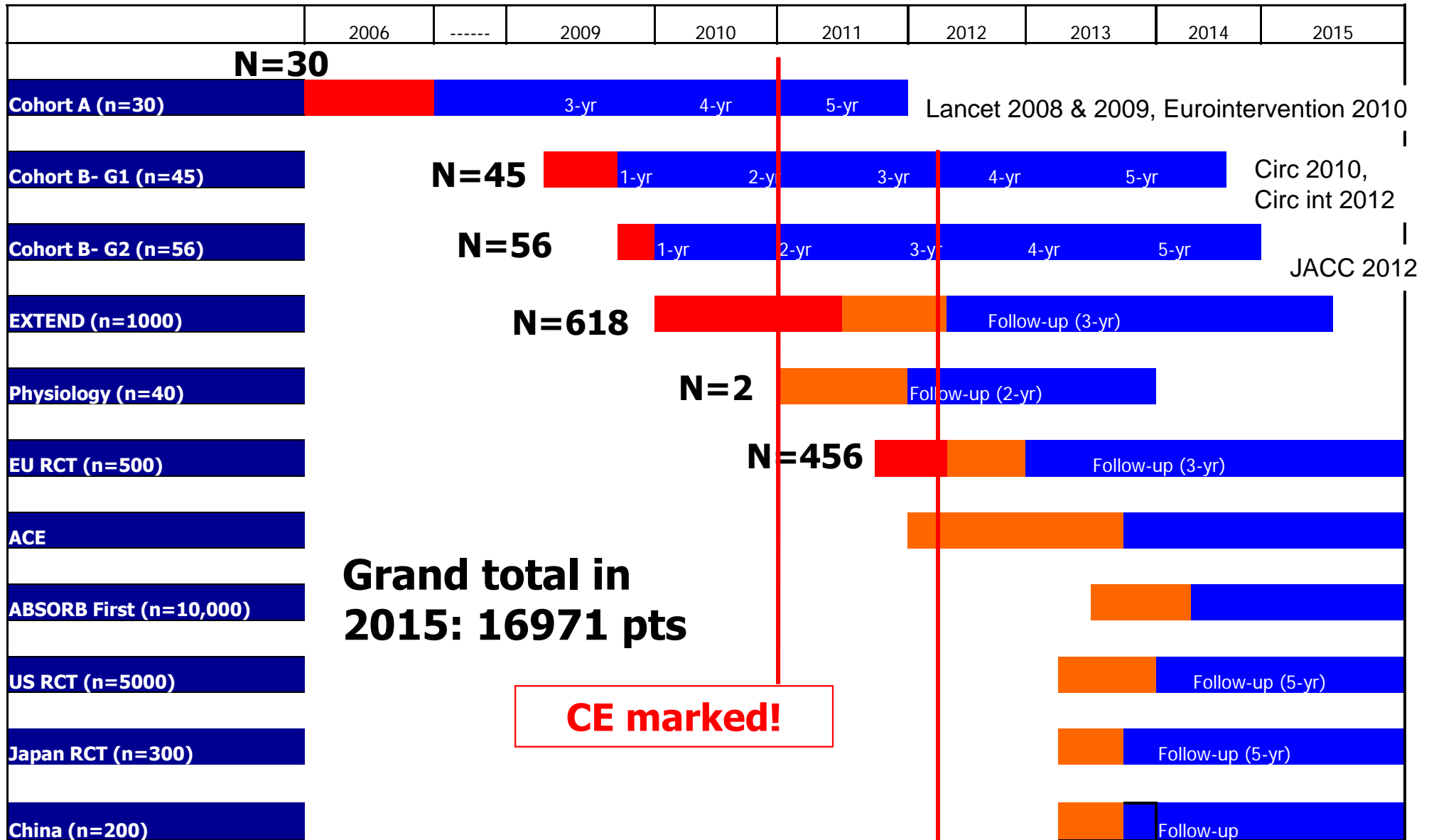


Gel-Permeate Chromatography



At 2 years the struts are still recognizable on OCT, while GPC showed a complete bioresorption of polymeric struts

Overview of ABSORB studies



Grand total in 2015: 16971 pts

CE marked!

Commercially available

Follow-up

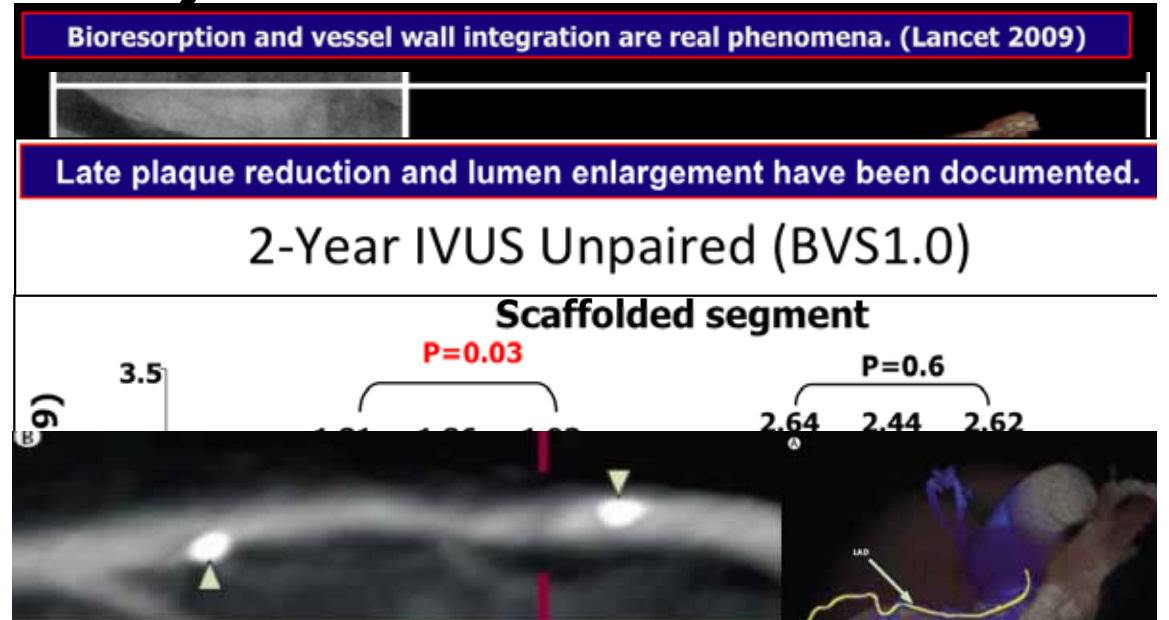
Enrolled

To be Enrolled

* Timelines based on patient follow-up dates, not data availability

What did we learn from ABSORB cohort A (2006-)?

- Bioresorption does occur
- Late enlargement of lumen, as a result of plaque shrinkage, has been documented
- Vasomotion and endothelial function can be restored in the scaffolded segment
- Stented lesion can be assessed by non-invasive imaging
- Restenosis and Thrombosis have not been seen up to 5 years, despite discontinuation of clopidogrel



Hierarchical	6 Months 30 Patients	12 Months 29 Patients*	3 Years 29 Patients*	5 Years 29 Patients*
Ischemia Driven MACE, %(n)	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Cardiac Death, %	0.0%	0.0%	0.0%	0.0%
MI, %(n)				
Q-Wave MI	0.0%	0.0%	0.0%	0.0%
Non Q-Wave MI	3.3% (1)**	3.4% (1)**	3.4% (1)**	3.4% (1)**
Ischemia Driven TLR, %				
by PCI	0.0%	0.0%	0.0%	0.0%
by CABG	0.0%	0.0%	0.0%	0.0%

No new MACE events between 6 months and 5 years
No stent thrombosis up to 5 years (All patients off clopidogrel)

*One patient withdrew consent after 6 months but the vital status of the patients and absence of cardiac event is known through the referring physician.

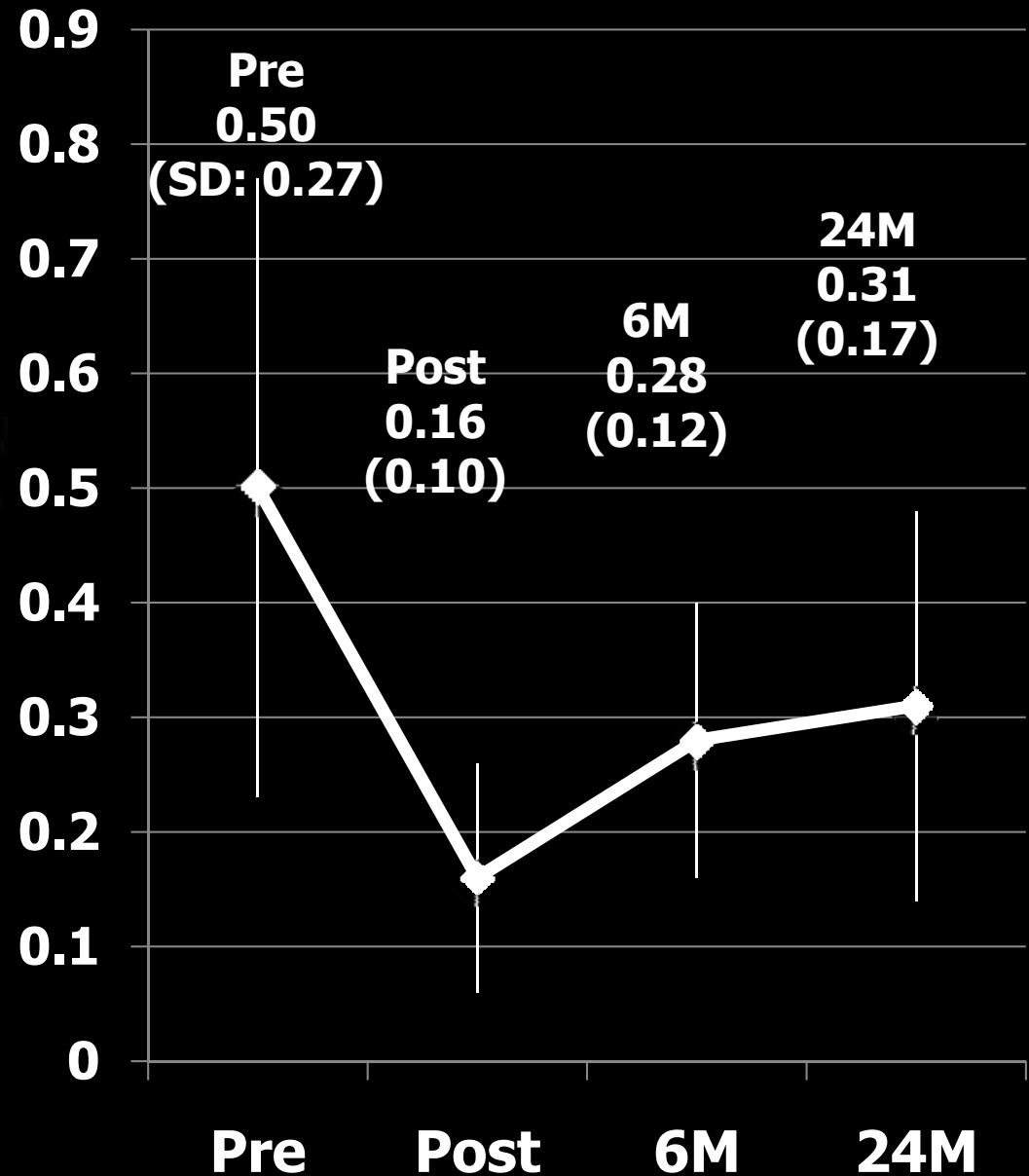
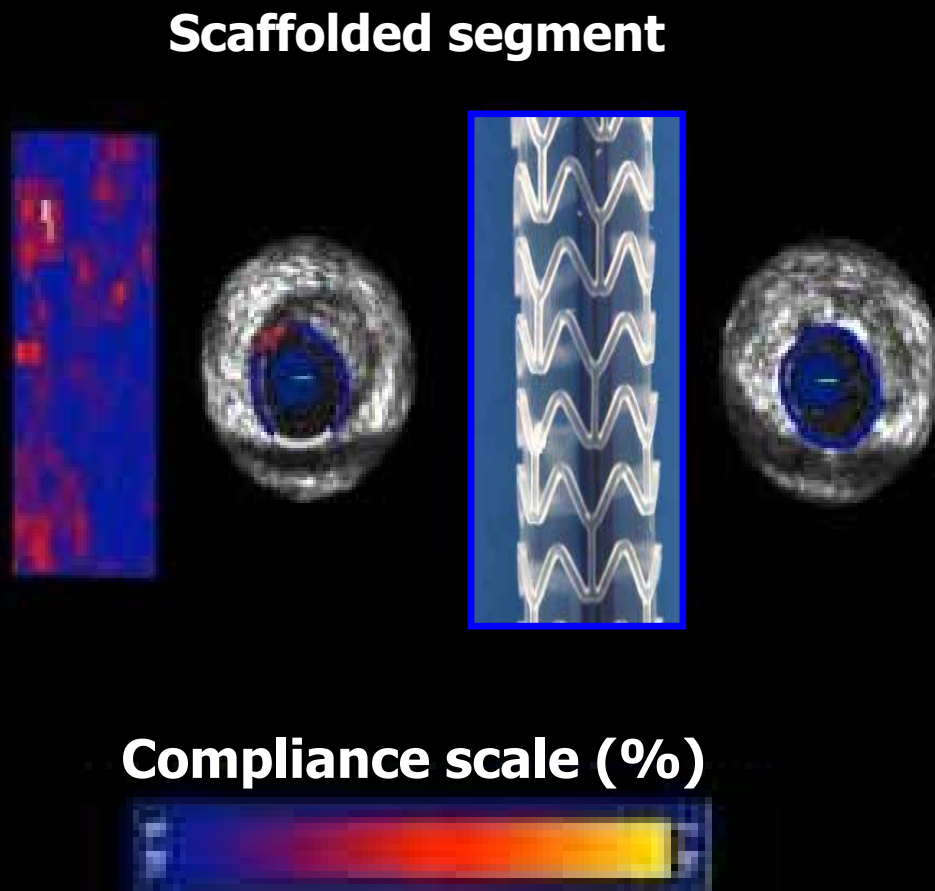
**This patient also underwent a TLR, not qualified as ID-TLR (DS = 42%) followed by post-procedural troponin qualified as non-Q MI and died from his Hodgkin's disease at 888 days post-procedure.

#What did we learn from cohort A and early FUP of cohort B?

Return of cyclic strain and mechano- transduction

● #6. . Reappearance of physiological (cyclic) strain after bioresorption

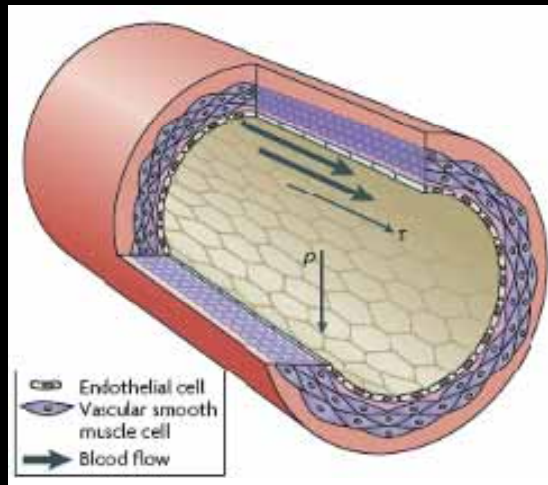
Pre, Post, 6 and 24 months after bioresorbable scaffolding



● #7. Impact of physiological cyclic strain and shear stress essential for the vessel wall biology

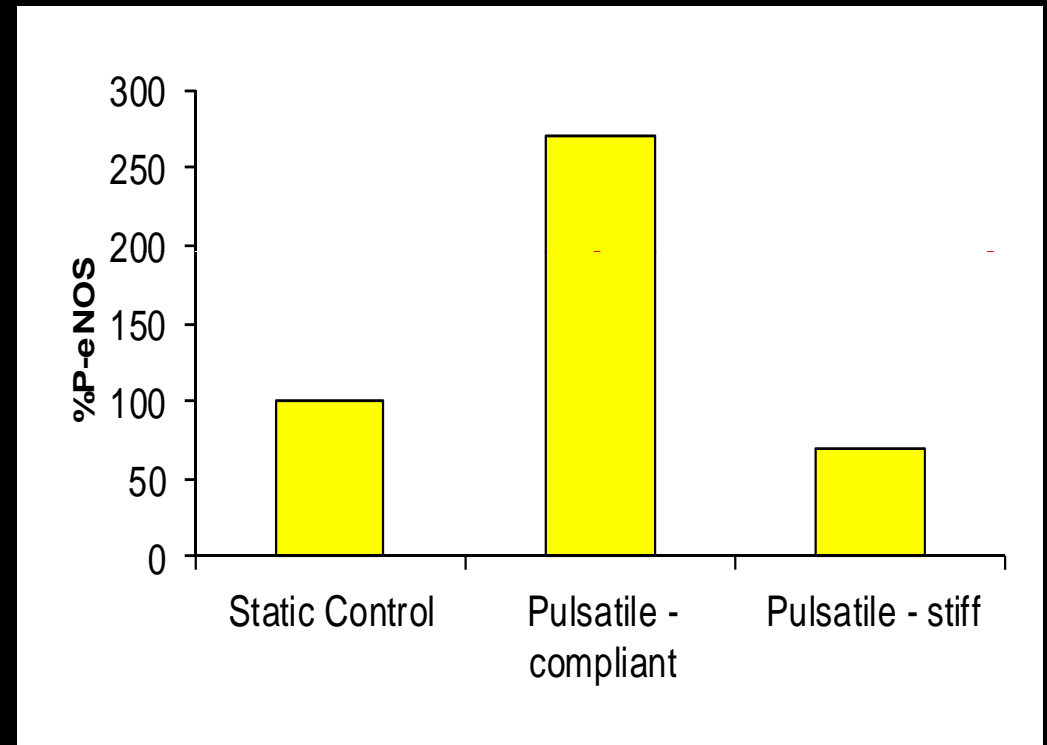
The translation of mechanical forces into chemical signals by cells is referred to as 'mechanotransduction'

Mechanical forces on the vessel wall



τ Shear Stress ρ Pressure

Hahn C and Schwartz M. *Nat Rev: Molec Cell Biol.* 2009;10:53-62.



↑↑Others

Normal responses to physiologic pulsatile cyclic strain and shear stress lead to cellular responses that stabilize the vessel

Gupta V and Grande-Allen K. *Cardiovasc Res.* 2006;72:375-383.

#What did we learn from cohort A and early FUP of cohort B?

Shielding of plaque at 2 and 5 years

“Golden tube”

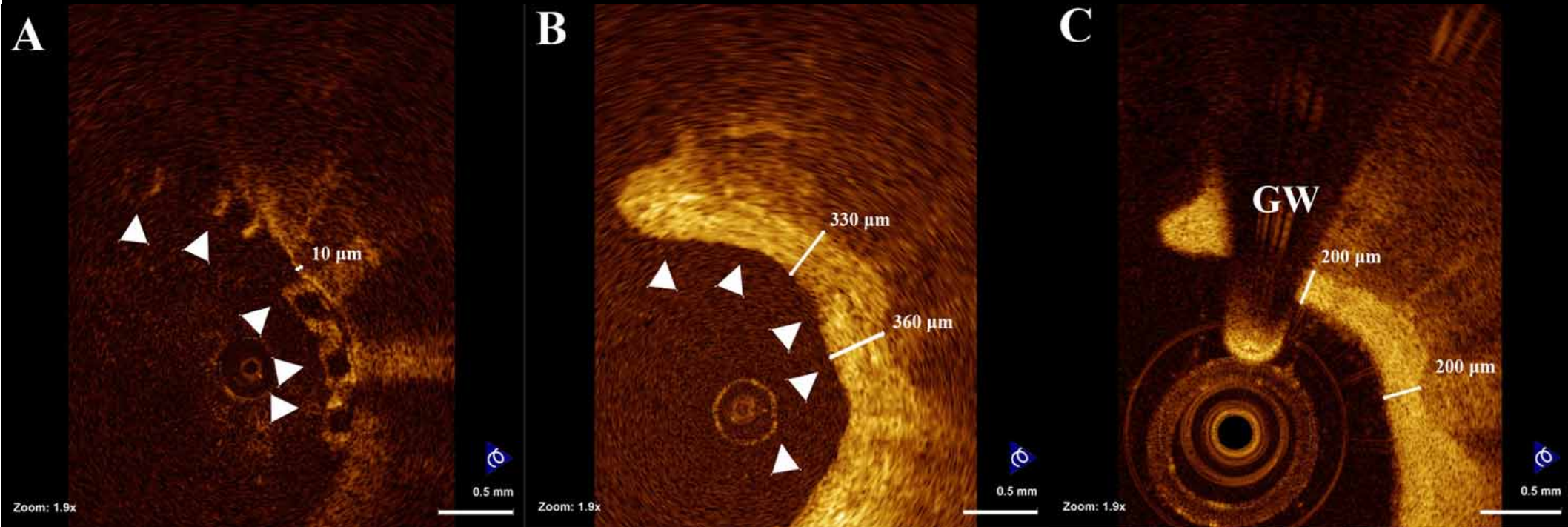
**(= late lumen enlargement on
OCT + with homogeneous
reflectivity of the light by the
endoluminal lining + vasomotion)**

**. Sealing and shielding of plaques as a result of scaffold implantation :
can the scaffold cap the plaque? 60 Months Follow up**

Baselines

6 months

60 months



Images in Cardiovascular Medicine

**Five-Year Optical Coherence Tomography Follow-Up of an
Everolimus-Eluting Bioresorbable Vascular Scaffold**

Changing the Paradigm of Coronary Stenting?

Antonios Karanasos, MD; Cihan Simsek, MD; Patrick Serruys, MD, PhD; Jurgen Ligthart, BSc;
Karen Witberg, CCRN; Robert-Jan van Geuns, MD, PhD; George Sianos, MD, PhD;
Felix Zijlstra, MD, PhD; Evelyn Regar, MD, PhD

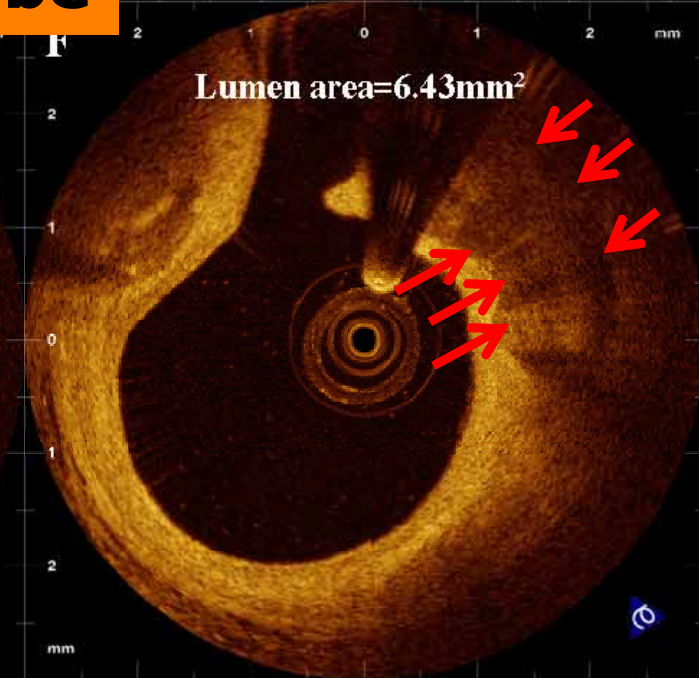
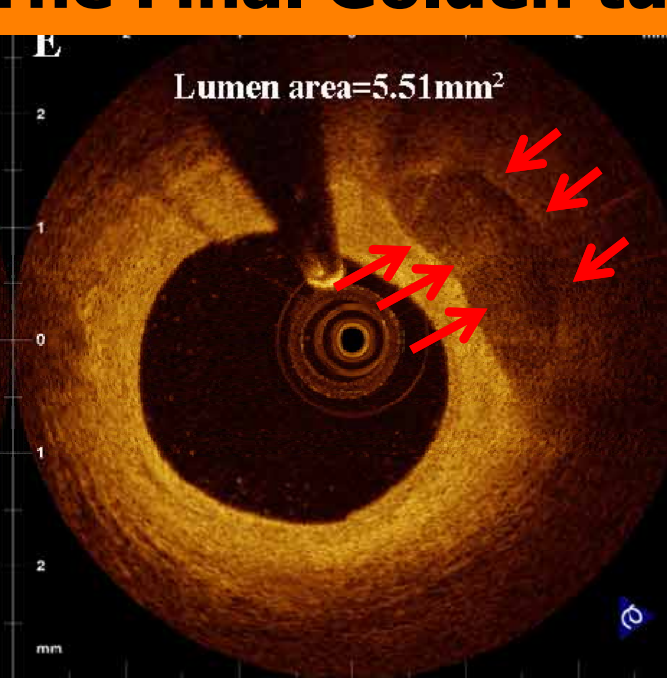
Sealing and shielding of plaques as a result of scaffold implantation : can the scaffold cap the plaque... and late lumen enlargement !!!

6 months



The Final Golden tube

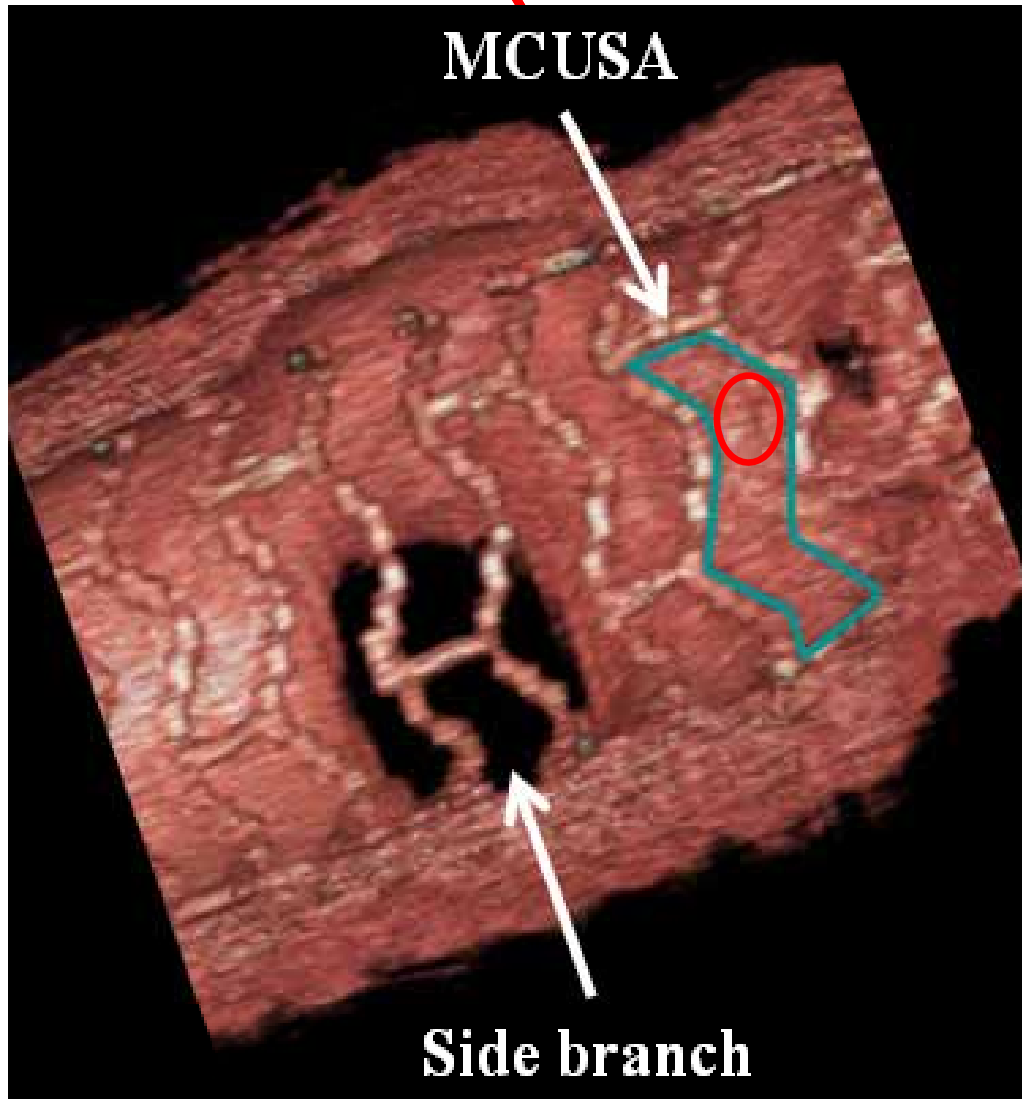
60 months



3-year imaging and clinical results of the ABSORB B

The second generation (BVS1.1) has a modified platform design and a different manufacturing process of the polymer.

Larger **Maximum Circular Unsupported scaffold area (MCUSA)**



Revision 1.1 has

- More radial strength
- More uniform support and drug application
- Longer duration of support

- Profile less than Cypher
- Track test better than ML Vision
- No change in strut thickness

ABSORB cohort B

Group B1 ($n = 45$)

QCA, IVUS, OCT, IVUS VH

**QCA, IVUS,
OCT, IVUS VH**

Baseline

6

Months

12

Months

18

Months

24

Months

36

Months

MSCT

Group B2 ($n = 56$)

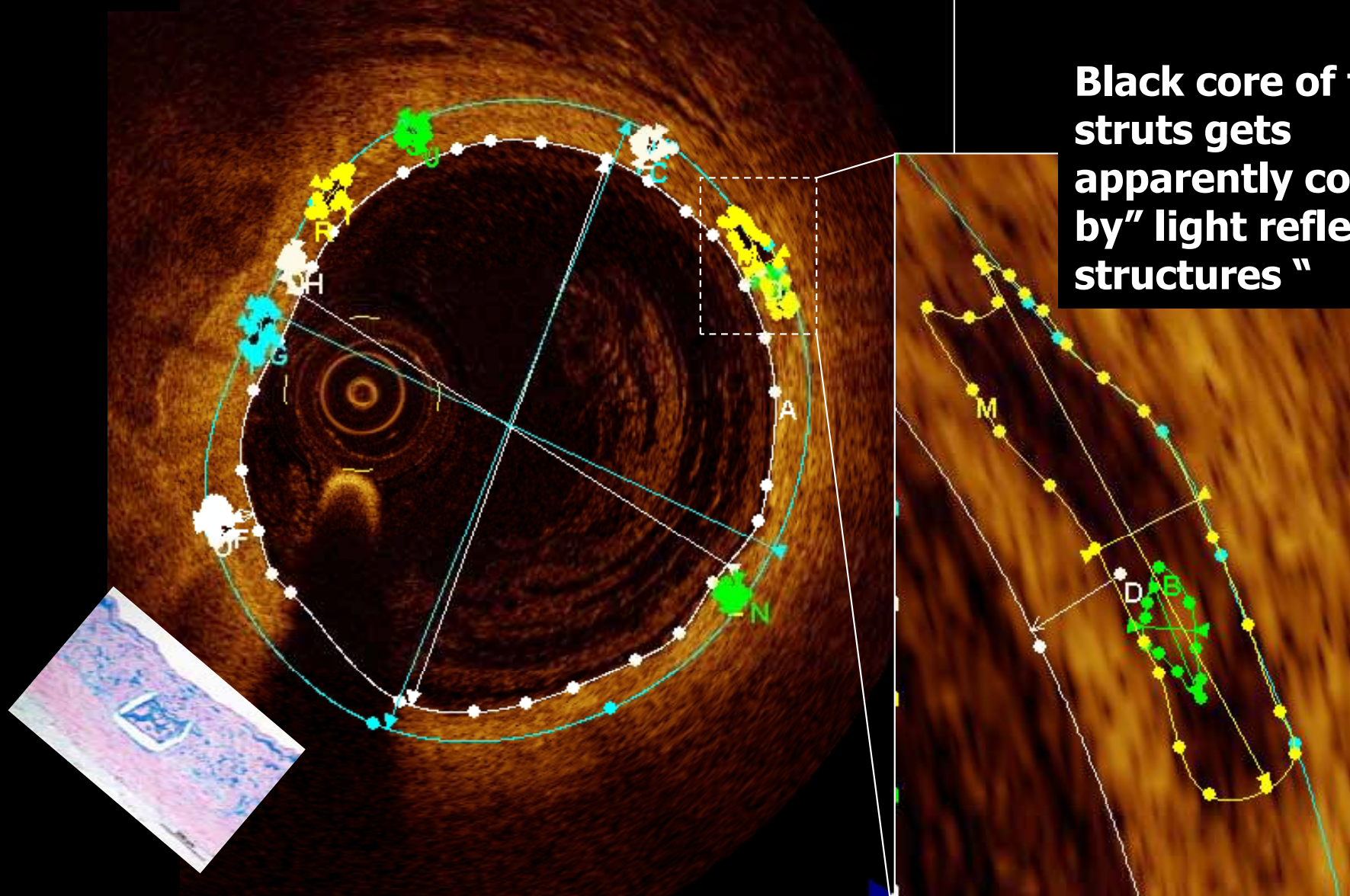
QCA, IVUS, OCT, IVUS VH

MSCT

- **Sponsor/ Funding: Abbott Vascular**
- **Primary Investigators:**
 - PW Serruys MD, PhD
 - J Ormiston MD
- **DSMB: J Tijssen PhD, M Wiemer MD, P Urban MD**
- **CEC: C Hanet MD, R Tölg MD, V Umans MD**
- **Angiographic, IVUS and OCT Corelab: Cardialysis**
- **Prospective, open label, FIM**
- **3.0 x 18mm devices to treat up to 2 lesions \leq 14mm in length**

- **12 sites Europe, Australia, New Zealand**
- **B de Bruyne, MD, PhD**
- **D Dudek, MD**
- **E Christiansen, MD**
- **P Smits, MD, PhD**
- **B Chevalier, MD**
- **D McClean, MD**
- **J Koolen, MD, PhD**
- **S Windecker, MD**
- **R Whitbourn, MD**
- **I Meredith, MD, PhD**
- **101 patients enrolled between 19 March and 6 November 2009**

Black core of the struts gets apparently colonized by "light reflecting structures"



	BL	1Y	3Y
Uncovered struts, %		3.25 ± 2.86	1.73 ± 1.53
≥2 consecutive cross-sections with at least one strut malapposed	0.27 ± 0.29 (n=16)	2.68 ± 1.63 (n=3)	0.64 ± 0.46 (n=3)

Temporal evolution of neointima, scaffold and lumen in human at 6, 12, 24 and 36 months

Circulation 2010

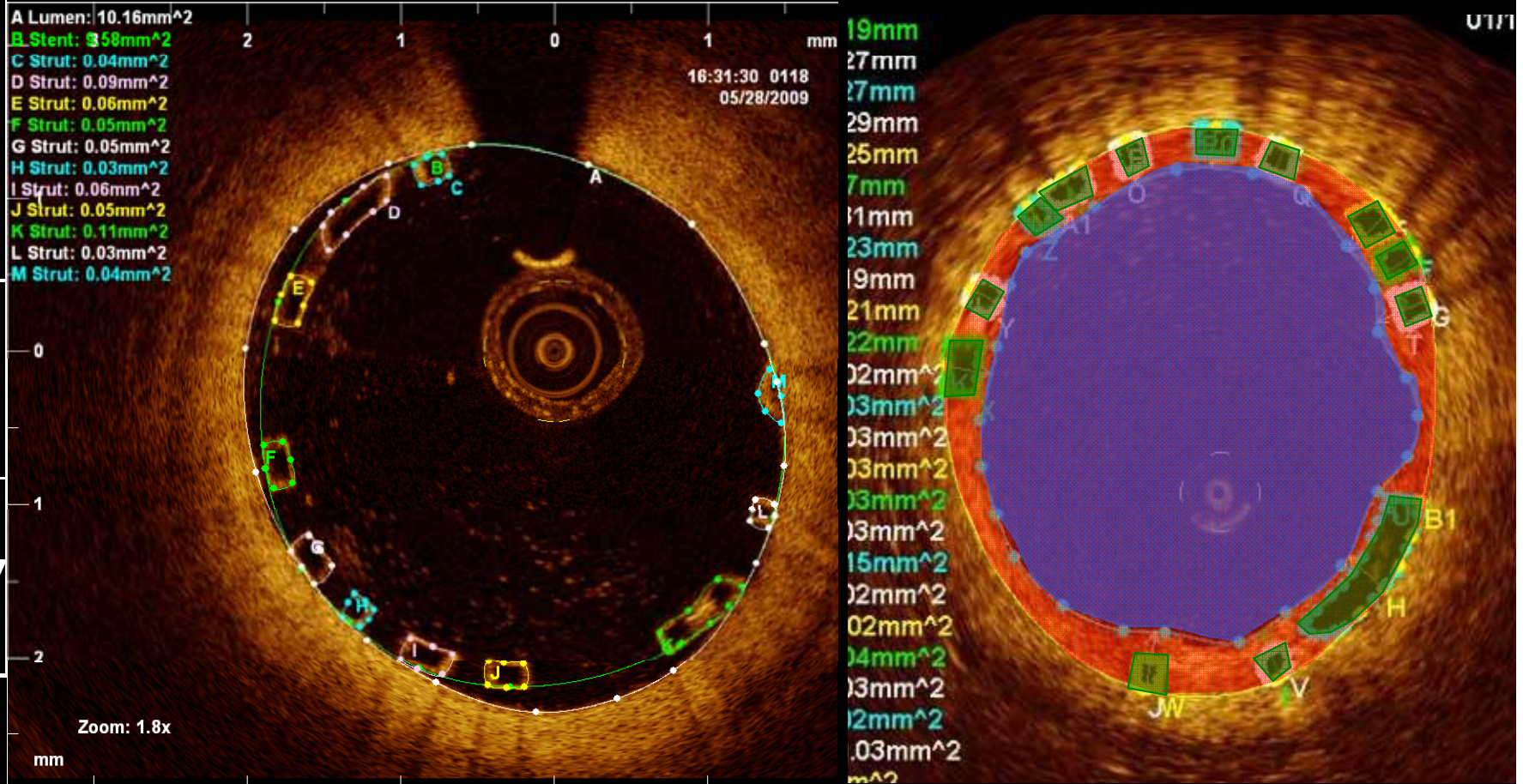
JACC 2011

Circ Int 2012

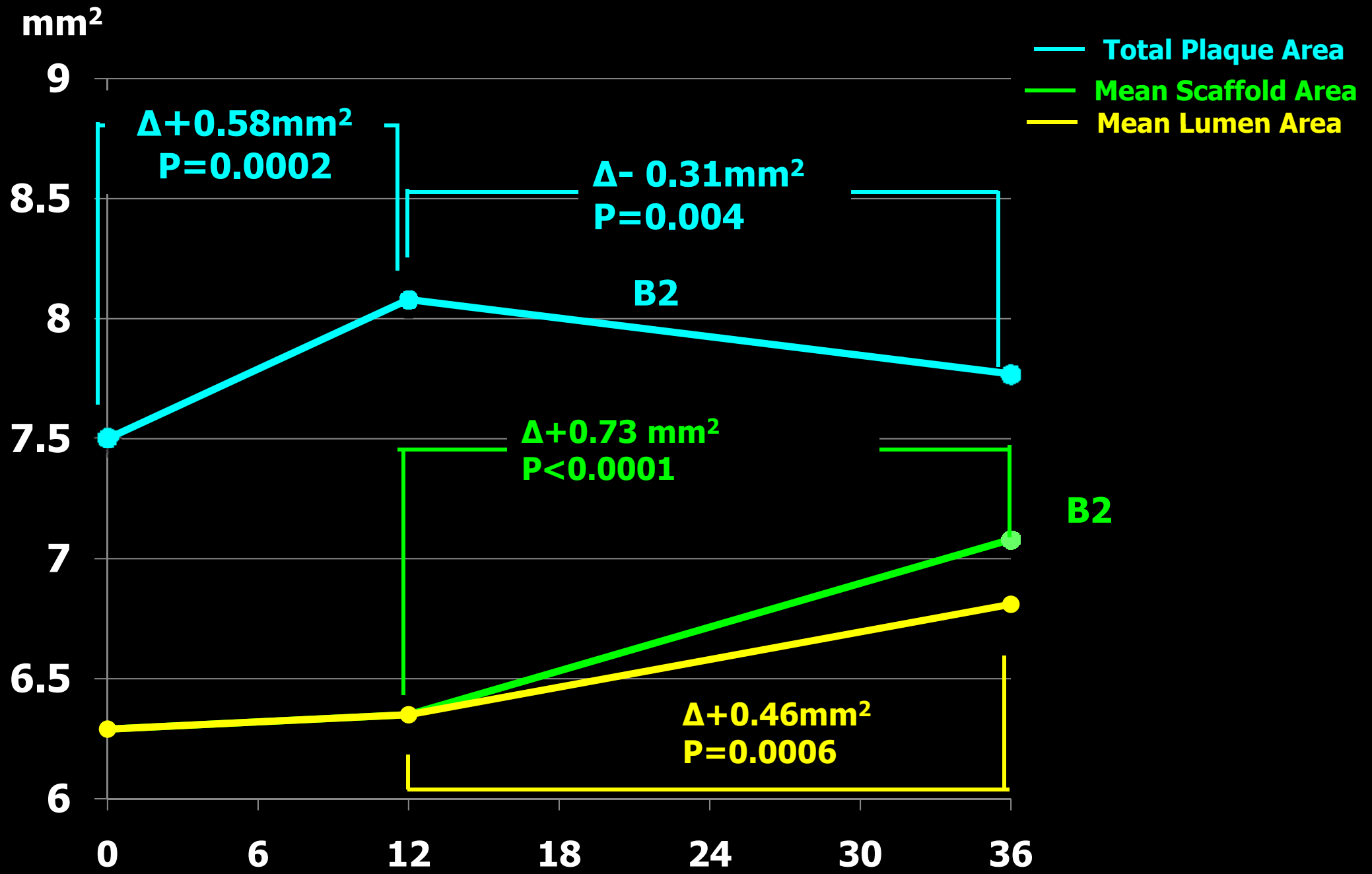
Mean Neointimal Thickness, micron

Scaffold area, mm²

Mean Lumen, mm²



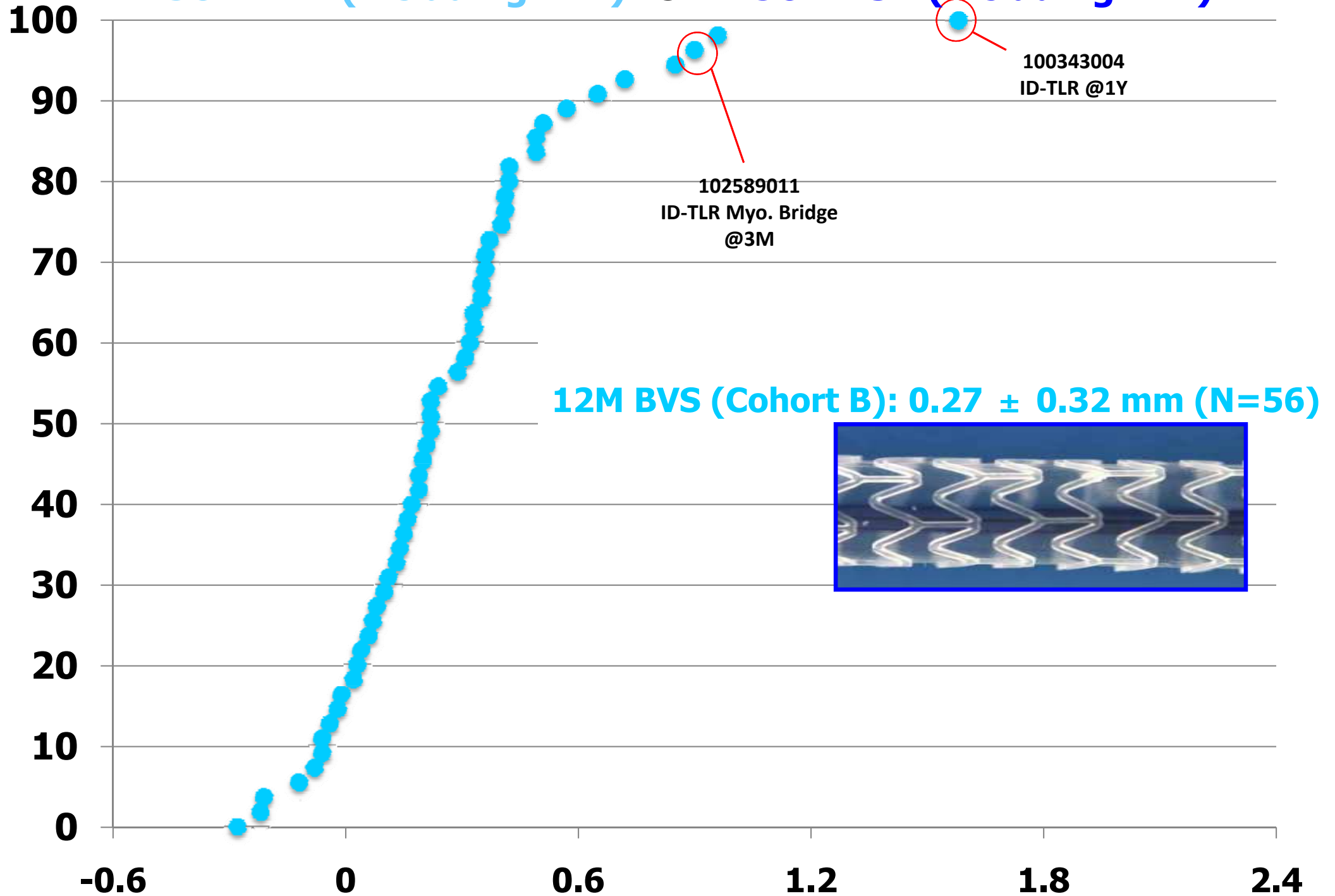
Results of Serial Quantitative IVUS Analysis (n=45)



Months

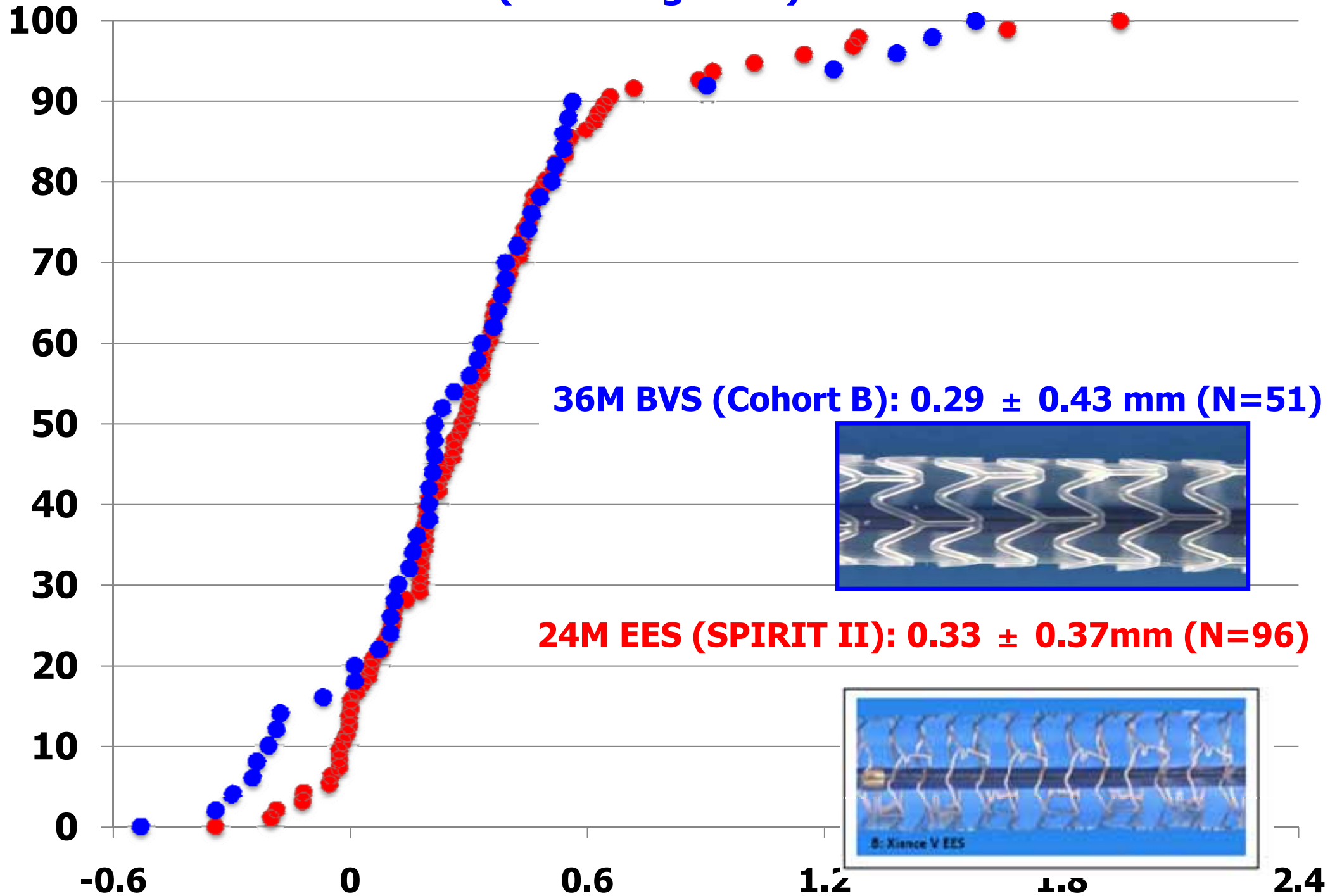
Insight on evolution of late luminal loss over times

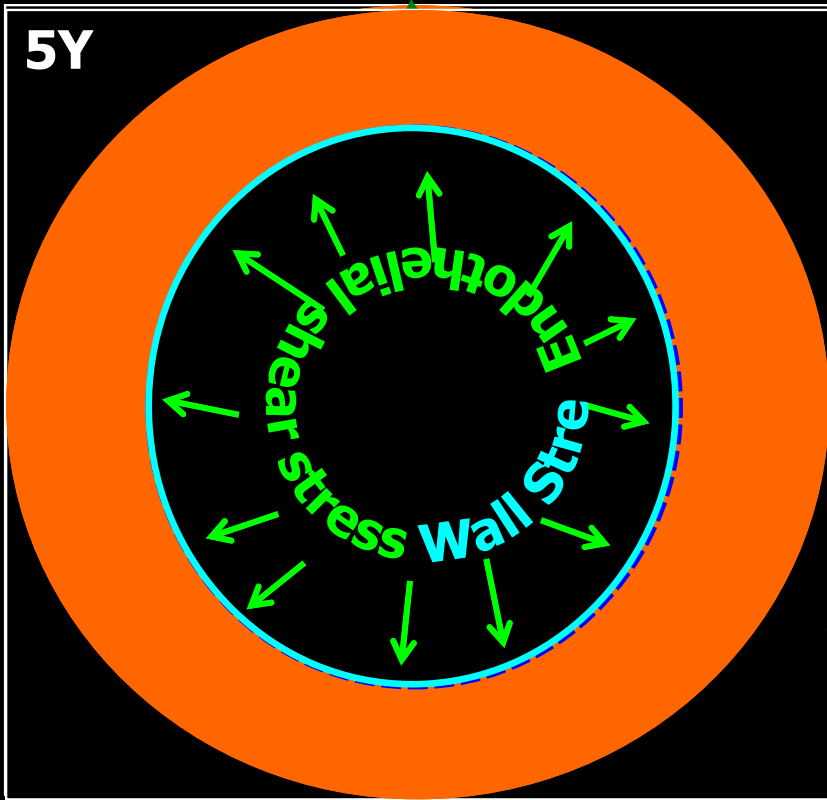
ABSORB 1Y (including TLR) vs. ABSORB 3Y (including TLR)



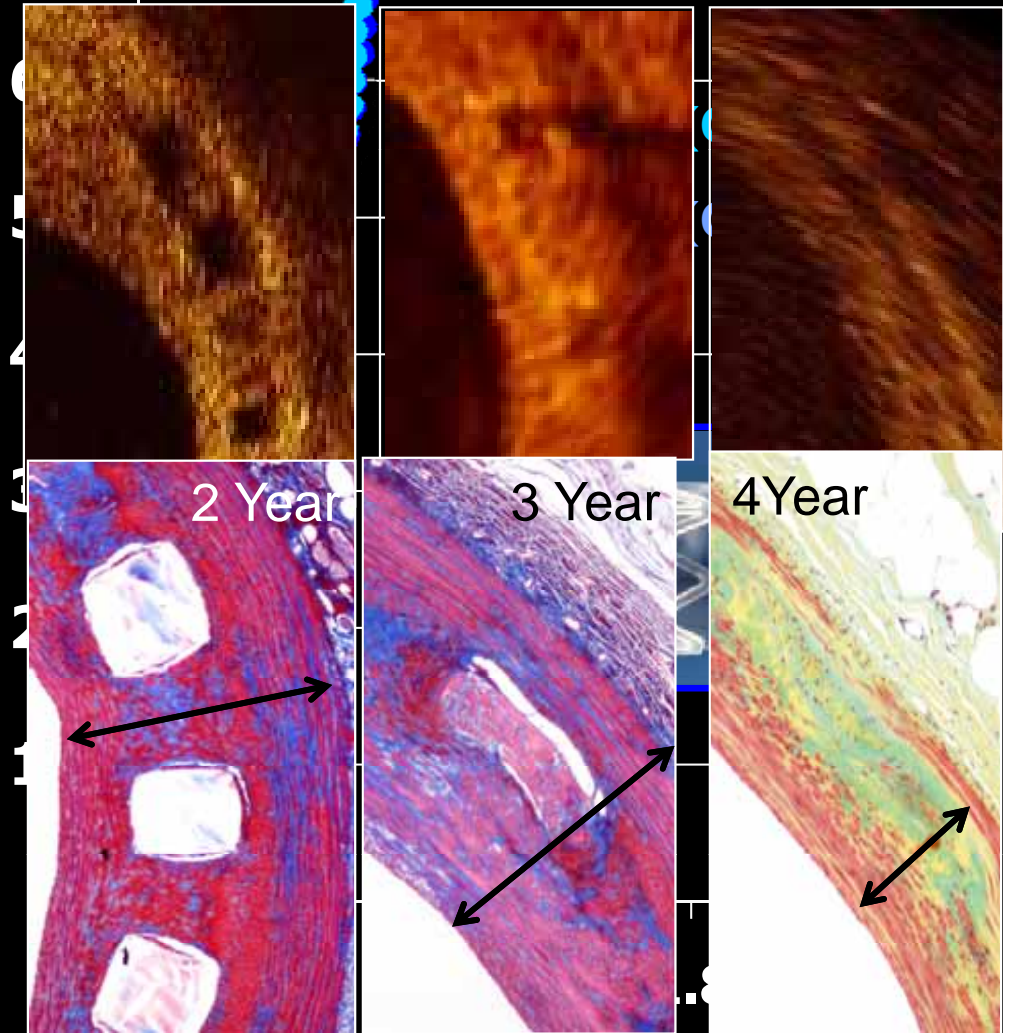
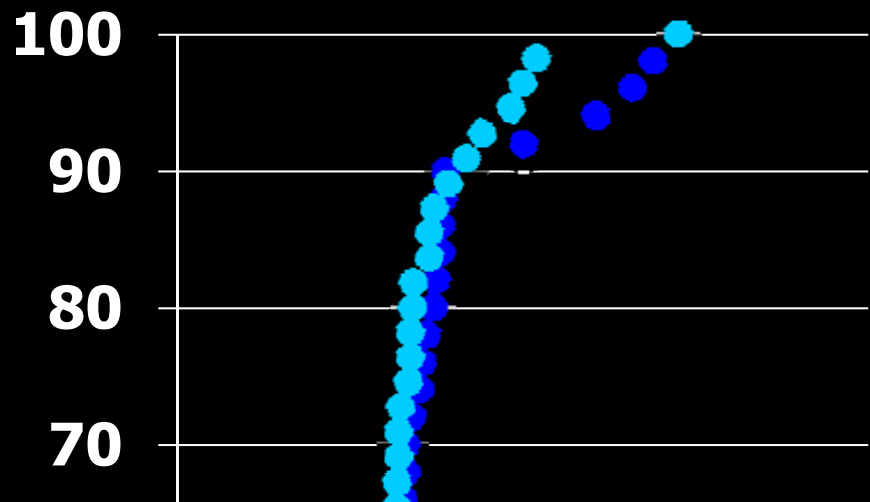
Insight on evolution of late luminal loss over times

ABSORB 3Y (including TLRs) vs. Xience 2Y





At 5 years, the vessel wall thinning (plaque media reduction?) will result in late lumen enlargement.



Conclusion

- **ABSORB cohort A (5 year FUP) demonstrated**
 - **Bioresorption of strut**
 - **Late lumen enlargement**
 - **Restoration of vasomotion**
 - **Feasibility of serial non-invasive follow-up**
 - **Long-term safety**
- **ABSORB cohort B (3 Year FUP) demonstrated**
 - **On OCT, enlargement of scaffold area that compensates for persistent increase of neointima**
 - **On IVUS, enlargement of scaffold area & lumen area with reduction of plaque area**
 - **On Angiography at 36 months, stable late loss over the last 24 months with vasodilation on intracoronary administration of nitrate**
 - **The 3-Y MACE rate of ABSORB is comparable to Xience (in a non-randomized post-hoc analysis)**